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January 20, 2004

Aric W. Ledford*

Registered Patent Agents -Karen R. Markowicz Nancy J. Leith Helene C. Carlson Gaby L. Longsworth Matthew J. Dowd Aaron L. Schwartz Mary B. Tung Katrina Y. Pei Quach Bryan L. Skelton Robert A. Schwartzman Timothy A. Doyde Jennifer R. Mahalingappa Teresa A. Collell Jeffrey S. Lundgren Victoria S. Rutherford Eric D. Hayes

Of Counsel Kenneth C. Bass III Evan R. Smith

*Admitted only in Maryland *Admitted only in Virginia •Practice Limited to Federal Agencies

WRITER'S DIRECT NUMBER: (202) 772-8637 INTERNET ADDRESS KARENM@SKGF.COM

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Re:

U.S. Utility Patent Application

Appl. No. 10/623,813; Filed: July 22, 2003

(Continuation-in-part of U.S. Appl. No. 09/720,086; § 102(e) date: July 23, 2001)

For: De novo DNA Cytosine Methyltransferase Genes, Polypeptides and Uses Thereof

Inventors: Li et al.

Our Ref: 0609.4560003/JAG/KRM/DJN

Sir:

The following documents are forwarded herewith for appropriate action by the U.S. Patent and Trademark Office:

- 1. Information Disclosure Statement;
- 2. Form PTO-1449 (19 sheets citing documents AA1-AC1, AL1-AM1, and AR1-AT19);
- 3. A copy of document AT17; and
- 4. One (1) return postcard.

It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier. In the event that extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned.

Sterne, Kessler, Goldstein & Fox PLLC.: 1100 New York Avenue, NW: Washington, DC 20005: 202.371.2600 f 202.371.2540: www.skgf.com

Commissioner for Patents January 20, 2004 Page 2

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Karen R. Markowicz
Agent for Applicants
Registration No. 36,351

KRM/DJN/cjs Enclosures

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Sterne, Kessler, Goldstein & Fox PLLC.: 1100 New York Avenue, NW: Washington, DC 20005: 202.371.2600 f 202.371.2540: www.skgf.com

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Li et al.

Appl. No. 10/623,813 Filed: July 22, 2003

For:

De novo DNA Cytosine Methyltransferase Genes,

Polypeptides and Uses Thereof

Art Unit: To Be Assigned Examiner: To Be Assigned

Atty. Docket:

0609.4560003/JAG/KRM/DJN

Information Disclosure Statement under 37 C.F.R. § 1.97(b)

Commissioner for Patents PO Box 1450 Alexandria, VA 22313-1450

Sir:

Listed on accompanying Form PTO-1449 are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98. A copy of document AT17 is provided.

A copy of documents **AA1** to **AC1** is not provided in accordance with the U.S. Patent and Trademark Office pre-OG notice of July 11, 2003, which states "[t]he Office hereby waives the requirement under 37 CFR 1.98 (a)(2)(i) for submitting a copy of each cited U.S. patent and each U.S. patent application publication for all U.S. national patent applications filed after June 30, 2003." Copies of all other documents were submitted to the Office in an IDS that complies with 37 C.F.R. § 1.98(a)-(c) in Application No. 09/720,086 (102(e) date: July 23, 2001), or cited by the Office during prosecution of said application which is relied upon for an earlier filing date under 35 U.S.C. § 120. Thus, copies of these documents are not attached. 37 C.F.R. § 1.98(d).

In accordance with 37 C.F.R. § 1.98(a)(3), Applicants' undersigned representative submits the following discussion of the relevance of the non-English language document AM1 cited on Form PTO 1449:

Document AM1 is in the Japanese language. An English language abstract of document AM1 is attached as document AT17. In addition, an English language abstract can also be found on the front of AM1. Applicants note that document AM1 was cited by the Examiner in parent application no. 09/720,086. In particular, in Paper No. 12, page 9, of the '086 application, the Examiner relied on accession no. AAT21884 on pages 991-992 of AM1 and provided an alignment of accession no. AAT21884 and SEQ ID NOS:1 and 3 from the '086 application. The alignment is cited on the PTO-1449 as document AR19.

Where the publication date of a listed document does not provide a month of publication, the year of publication of the listed document is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the month of publication is not in issue. Applicants have listed publication dates on the attached PTO-1449 based on information presently available to the undersigned. However, the listed publication dates should not be construed as an admission that the information was actually published on the date indicated.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

This statement should not be construed as a representation that a search has been made, or that information more material to the examination of the present patent

application does not exist. The Examiner is specifically requested not to rely solely on the material submitted herewith.

This Information Disclosure Statement is being filed before the mailing date of a first Office Action on the merits. No statement or fee is required.

It is respectfully requested that the Examiner initial and return a copy of the enclosed PTO-1449, and indicate in the official file wrapper of this patent application that the documents have been considered.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

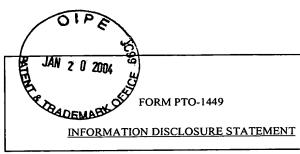
Karenk. Marliodicz

Karen R. Markowicz Agent for Applicants Registration No. 36,351

Date: January 20, 2004

1100 New York Avenue, N.W. Washington, D.C. 20005-3934 (202) 371-2600

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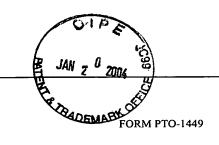
APPLICANT
Li et al.

FILING DATE
July 22, 2003

APPLICATION NO.
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	AA1	5,578,7	16	11/26/1996	Szyf et al.	ļ		12/01/1993		
	AB1	6,183,9	68 B1	02/06/2001	Bandman et al.	 	<u> </u>	03/25/1999		
	AC1	6,492,1	68 B1	12/10/2002	Kladde et al.	 		04/22/1999		
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OTHER (INCIDENT	AR	<u>1</u>	Aoki. A., <i>et al.</i> , "Er	zymatic properties	s of <i>de novo-</i> type mouse DNA (cytosinss (September 2001)	ne-5) methyl	transferases," Nuc	l. Acids Res.		
	AS	1	Ariel, M., et al., "G Nature Publishing (Ariel, M., et al., "Gamete-specific methylation correlates with imprinting of the murine Xist gene," Nat. Genet. 9:312-315 Nature Publishing Group (1995)						
	АТ	1	Ausubel, F.M., et a Molecular Biology,	subel, F.M., et al., eds., "Expression of Proteins in Insect Cells Using Baculoviral Vectors," in Current Protocols in lecular Biology, Greene Publishing Associates and Wiley-Interscience, New York, NY, pp. 16.8.1-16.11.7 (1990)						
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INFORMATION DISCLOSURE STATEMENT

SKGF Rev. 1/95 U.S. PATENT DOCUMENTS **EXAMINER** SUB-CLASS FILING DATE CLASS NAME INITIAL DOCUMENT NUMBER DATE AA AB AC AD ΑE ΑF ΑG ΑH ΑI ΑJ ΑK FOREIGN PATENT DOCUMENTS **EXAMINER** TRANSLATION DOCUMENT NUMBER DATE COUNTRY **CLASS** SUB-CLASS INITIAL Yes No AL Yes No AM Yes No AN Yes No ΑO Yes AP OTHER (Including Author, Title, Date, Pertinent Pages, etc.) Bachman, K.E., et al., "Dnmt3a and Dnmt3b Are Transcriptional Repressors That Exhibit Unique Localization Properties to Heterochromatin," J. Biol. Chem. 276:32282-32287, The American Society for Biochemistry and Molecular Biology, Inc. AR 2 (August 2001) Baylin, S.B., et al., "Alterations in DNA Methylation: A Fundamental Aspect of Neoplasia," Adv. Cancer Res. 72:141-196, AS <u>2</u> Academic Press (February 1998) Bestor, T., et al., "Cloning and Sequencing of a cDNA Encoding DNA Methyltransferase of Mouse Cells," J. Mol. Biol. ΑT 2 203:971-983, Academic Press (1988) DATE CONSIDERED **EXAMINER EXAMINER**: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not

July 22, 2003

considered. Include copy of this form with next communication to Applicant.

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	AR	<u>3</u>		vation of mamn	nalian DNA methyltransferase b Press (1992)	y cleavage of a Zn bi	nding regulatory d	lomain," <i>EMBO J</i> .
	AS	<u>3</u>	Brandeis, M., et al. 12:3669-3677, Oxi	., "The ontogengord University	y of allele-specific methylation a Press (1993)	associated with imprit	nted genes in the r	nouse," <i>EMBO J</i> .
	AT	3	Brockdorff, N., "C W., and Surani, A.	onvergent them, eds., Oxford U	es in X chromosome inactivatio Iniversity Press, Oxford, UK, pp	n and autosomal impro. 191-210 (December	inting," in <i>Genom</i> 1997)	ic Imprinting, Reil

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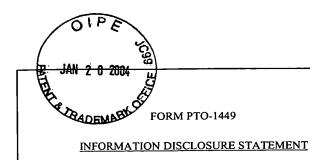
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	AR	4	Chaillet, J.R., et al. Progressively Char	, "Parental-Speci ges during Embr	fic Methylation of an Impryogenesis," Cell 66:77-83,	rinted Transgene in , Cell Press (1991)	ı Establ	ished during Gam	etogenesis and
	AS	4	Chen, T., et al., "A Novel Dnmt3a Isoform Produced from an Alternative Promoter Localizes to Euchromatin and Its Expression Correlates with Active de Novo Methylation," J. Biol. Chem. 277:38746-38754, The American Society for Biochemistry and Molecular Biology, Inc. (October 2002)						
	AT	4	Cheng, X., "Structure and function of DNA methyltransferases," Annu. Rev. Biophys. Biomol. Struct. 24:293-318, Annual Reviews, Inc. (1995)						
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ATTY. DOCKET NO. 0609.4560003/JAG/KRM/DJN	APPLICATION NO. 10/623,813
APPLICANT Li et al.	
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	AR	<u>5</u>	Finnegan, E.J., and from Arabidopsis to	Dennis, E.S., "Iso haliana," Nucl. Aci	lation and identification by sequer ids Res. 21:2383-2388, Oxford Ur	nce homology of hiversity Press (1	a putative cytosin 993)	e methyltransferase	
	AS	<u>5</u>	Flynn, J., et al., "Murine DNA Cytosine-C ⁵ Methyltransferase: Pre-Steady- and Steady-State Kinetic Analysis with Regulatory DNA Sequences," <i>Biochem.</i> 35:7308-7315, American Chemical Society (1996)						
	АТ	<u>5</u>	Flynn, J., et al., "DNA Binding Discrimination of the Murine DNA Cytosine-C ⁵ Methyltransferase," J. Mol. Biol. 279:101-116, Academic Press (May 1998)						
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	AR	<u>6</u>	Hata, K., et al., "D in mice," Develop.	nmt3L cooperate <i>129</i> :1983-1993,	es with the Dnmt3 family o Company of Biologists Ltd	f de novo DNA methyl d. (April 2002)	ransferases to estab	lish maternal imprints
	AS	<u>6</u>	Jähner, D., and Jae Biological Signific	nisch, R., "DNA ance, Razin, A.,	. Methylation in Early Man eds., Springer-Verlag, Nev	nmalian Development," v York, NY, pp. 189-21	in <i>DNA Methylatio</i> 9 (1984)	n. Biochemistry and
	AT	<u>6</u>	Jentsch, S., et al., (1981)	"DNA methylt	ransferases affecting the s	sequence 5'CCGG," A	ucl. Acids Res. 9:2	753-2759, IRL Press
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	AR	7	Jones, P.A., and Natl. Acad. Sci.	l Gonzalgo, M.L. USA 94:2103-21	, "Altered DNA methylation a 05, National Academy of Sci	and genome instabili ences (March 1997)	ty: A new pathwa	ay to cancer?," Proc.
	AS	7	Klimašauskas, S IRL Press at Ox	S., et al., "The se ford University	quence specificity domain of Press (1991)	cytosine-C5 methlas	es," Nucl. Acids i	Res. 19:6183-6190,
	AT	7	Kumar, S., et a.	<i>l.</i> , "The DNA (cy	tosine-5) methyltransferases,	" Nucl. Acids Res. 22	:1-10, Oxford Ui	niversity Press (1994)
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	AR	8	Laird, P.W., and J 30:441-464, Annu	Jaenisch, R., "Th aal Reviews Inc.	e Role of DNA Methylation in Cance (1996)	r Genetics a	and Epigenetics,"	Annu. Rev. Genet.	
	AS	<u>8</u>	Lauster, R., et al., "Cytosine-specific Type II DNA Methyltransferases. A Conserved Enzyme Core with Variable Target-recognizing Domains," J. Mol. Biol. 206:305-312, Academic Press Ltd. (1989)						
	AT	8	Lazar, E., et al., " Biological Activi	Lazar, E., et al., "Transforming Growth Factor a: Mutation of Aspartic Acid 47 and Leucine 48 Results in Different Biological Activities," <i>Mol. Cell. Biol. 8</i> :1247-1252, American Society for Microbiology (1988)					
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	AR	Lei, H., et al., "De novo DNA cytosine methyltransferase activities in mouse embryonic stem cells," <i>Development 122</i> :3195-3205, The Company of Biologists Ltd. (1996)						
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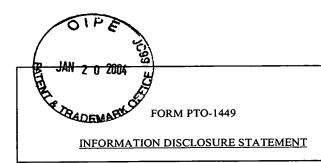
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APPLICANT Li et al.	
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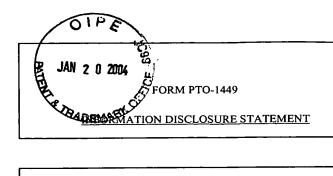
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	AR	10	Li, E., "Role o Oxford Univer	of DNA methylationsity Press, Oxford	on in mammalian developmen I, UK, pp. 1-20 (December 19	t," in <i>Genomic Imprii</i> 197)	nting, Reik, W., a	and Surani, A., eds.,		
	AS	<u>10</u>	Malagnac, F., of Eukaryotic	Malagnac, F., et al., "A Gene Essential for De Novo Methylation and Development in Ascobolus Reveals a Novel Typof Eukaryotic DNA Methyltransferase Structure," Cell 91:281-290, Cell Press (October 1997)						
	AT	<u>10</u>	Narayan, A., e Wiley-Liss, In	Narayan, A., et al., "Hypomethylation of Pericentromeric DNA in Breast Adenocarcinomas," Int. J. Cancer 77:833-838 Wiley-Liss, Inc. (September 1998)						
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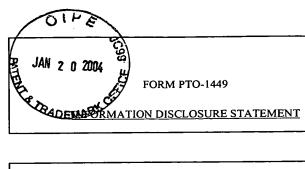
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	AR	13	Razin, A., and Biological Sig	Cedar, H., "DNA nificance, Jost, J.P	methylation and embryogensis	s," in <i>DNA Methylat</i> user Verlag, Basel,	ion: Molecular B Switzerland, pp.	tiology and 343-357 (1993)	
	AS	<u>13</u>	Reid, G.K., et Curr. Opin. M	al., "Selective inhi	ibition of DNA methyltransfera 7, Current Drugs (April 2002)	ase enzymes as a no	vel strategy for c	ancer treatment,"	
	АТ	13	Robertson, K. normal tissues	D., <i>et al.</i> , "The hur and overexpression	man DNA methyltransferases (on in tumors," <i>Nucl. Acids Res</i> .	DNMTs) 1, 3a and 27:2291-2298, Oxf	3b: coordinate m ord University P	RNA expression in ress (June 1999)	
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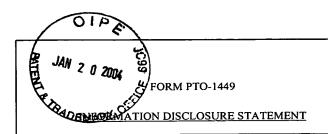


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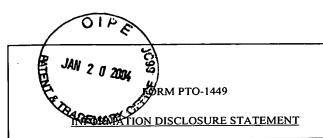
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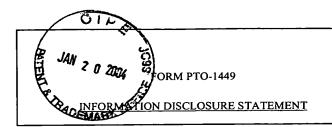
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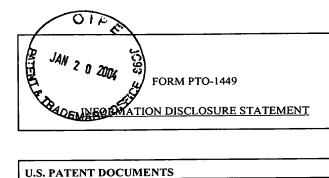
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	AT	18	GenCore nucleic acid and amino acid database. Sequence comparison between accession number AF067972 from Gene 1999 paper and Applicants' SEQ ID NO: 7 and 8, February 12, 2001						
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	AR 19 GenCore nucleic acid database. Sequence comparison between accession number AAT21884 from WO document 9514772-A1 and Applicants' SEQ ID NO: 1 and 3, June 1, 1995								
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